modifying the nucleic acid segment sufficient to modulate the result of expression of the drug target protein in the cells, tissue or organ; and,

introducing the modified nucleic acid segment into the cells, tissue or organ under somatic cell gene transfer conditions sufficient to express a modified drug target protein; and,

administering to the cells, tissue or organ, a candidate drug compound; wherein,

the candidate drug compound modulates expression of the modified drug target protein; and,

analyzing the expression of the modified drug target protein in cells, tissue or organ to which the candidate drug has been administered to determine potential drug target proteins.

REMARKS

Page 21, lines 23-24, of the specification has been amended to comply with MPEP §608.01, *i.e.* delete reference to the hyperlink. No new matter is added by virtue of this amendment.

Claims 1, 2, 7, 14, 29 and 31 have been amended to comply with the Examiner's recommendations. Support for these amendments can be found throughout the specification. For example, measuring the activity of an over-expressed or under-expressed ion-channel protein is discussed on page 11, lines 26 to 29 through to page 12 lines 1-2; page 13, lines 25 to 30 through to page 15, lines 1 to 27; Examples 1 to 8. No new matter is added by virtue of these amendments and their entry is respectfully requested.

Claim 1-15 and 29-31 were rejected under 35 U.S.C. § 112, second paragraph. The rejection is traversed.

Claim 1 has been amended to define the term "selected protein" and "selected cells" to define the protein as the drug target protein and the cells as those cells used for the somatic gene

transfer of the nucleic acid encoding the drug target protein. The detailed methods and materials used are found in Examples 1-8 and throughout the specification.

Claim 1 also has been amended to further recite the method. Support for the amendment is found throughout the specification, in particular, page 5, lines 3-28 (general description of the steps); page 6, lines 19-29 (description of one type of activity e.g. "mimicking"); page 7, lines 1-25 (examples of drug target proteins and somatic cell gene transfer techniques); page 8, lines 1-10 (general description of cells that can be selected for use in the invention); page 9, lines 1 to 24 (description of result, activity or expression); page 24, lines 29-30 through to page 25, lines 1 to 8 (description of different activities of drug target proteins); page 10, lines 19 to 31 through to page 11, lines 1 to 13 (examples of description of drug target proteins).

To expedite prosecution, claims 2, 7, 14, 29 and 31 also have been amended to provide further clarity.

In view thereof, reconsideration and withdrawal of the rejection is requested.

Claim 31 also was rejected under 35 U.S.C. 101 on grounds that the claim does not recite proper method steps.

Applicant respectfully disagrees. The format of claim 31 is acceptable. Nevertheless, to expedite prosecution, the claim has been amended without substantive limitation to obviate the rejection. Withdrawal of the rejection is requested.

Claims 1-15 and 29-31 were rejected under 102(e) over Kamb (U.S. Patent No. 5,955,275)."

As grounds for the rejection, it is alleged that the perturbagens reported in Kamb can be considered "selected" or "target" proteins; can exert their effect "by forming a binding

complex"; "this binding complex ... is expected to behave in a manner similar to a small molecule inhibitor of the wild type protein"; produce "dominant-negative" effects; and can be identified "by standard techniques."

However, as specifically acknowledged on page 8 of the Office Action (emphasis added):

> A perturbagen functioning in such a manner and selected for its ability to increase or decrease **the expression of a reporter protein** would necessarily be selected based on its ability to 'mimic' or 'predict' the effect [of] a drug."

The rejection is traversed.

Applicant's invention includes use of somatic gene cell transfer methods of molecules encoding a potential drug target protein and the expression of which may be modulated by a candidate drug compound. Applicant does not require use of a "**pseudo-genetic** approach" (cf. Kamb, column 8, lines 26 to 28). Applicant **does not require use a secondary** means for measuring any potential effects of a candidate drug on a drug target protein's expression, whereas Kamb "reads" the effects of a perturbagen by measuring reporter protein expression (see Kamb at the Abstract; column 3, lines 1-26). Kamb at column 3, lines 29-31 further states that:

> "[t]he **reporter serves as a surrogate for the cellular phenotype** and thus **must be chosen carefully** to reflect the relevant phenotypic **state as closely as possible**." (Emphasis added).

In contrast, Applicant **does not require use a secondary or surrogate** source for the cellular phenotype and **does not have to carefully choose nor approximate the phenotypic state as closely as possible.** Applicant's methods are direct using the potential drug target protein, do not require substitution of the expression of a drug target protein with the expression of a reporter and therefore, **do not** require close approximation of the phenotypic state. See for example page 4, lines 25-30, through to page 18, lines 1-25 of the appiication.

Indeed, Kamb clearly *teaches away* from Applicant's invention. That is, Kamb reports a **secondary** means of measuring the expression of a perturbagen. As stated in Kamb, column 8, lines 23-28:

> "Sequences are isolated from the expression library based on their ability to alter the activity of the cis regulatory sequence, **as read out by the reporter expression level.** The method thus comprises a set of tools and techniques that together permit the identification of components of genetic pathways **using a pseudo-genetic approach**." (Emphasis added).

As mentioned, Applicant does not require such "pseudo-genetic" techniques, but instead somatic gene transfer, which is a genetic technique. The drug target protein introduced into host cells via this method and a candidate drug compound that modulates the expression of the drug target protein is not measured by secondary means as taught by Kamb, i.e. Applicant does not require use reporter gene expression to approximate a cellular phenotype as closely as possible.

The Kamb document also reports that the sequences of the perturbagens are based on their ability to "alter the activity of the cis regulatory sequence," (Kamb, column 8, lines 24-25).

Respectfully, based on such disclosure, the conclusions alleged in the Office Action that "perturbagens" "mimic" or "predict" and have a "dominant effect" are inaccurate. The Office Action allegation appears to extrapolate well beyond the disclosure of Kamb, especially when Kamb states that the reporter gene has **to closely approximate** the phenotype.

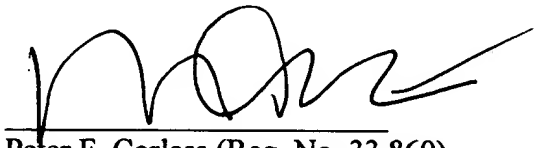
Kamb, does not, therefore, teach every element of Applicant's claims and the rejection is properly withdrawn. In this regard, attention is directed to Section 2131 of the Manual of Patent Examining Procedure, which states in part:

A claim is anticipated only if and each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Brothers. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the .. claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

In view thereof, reconsideration and withdrawal of the rejection are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES

In the Specification:

Page 21, lines 23-24, has been amended as follows:

(AMENDED) Genbank is also available on the internet. ~~at http://www.ncbi.nlm.nih.gov.~~

In the Claims:

1. (amended) A method for predicting the effect of a drug candidate compound, comprising:

[a)] modulating, by somatic gene transfer, expression of a drug target protein in host cells; wherein, [a selected protein in selected cells; and

b) analyzing the result of expression of the protein to thereby predict the effect of the drug candidate compound

expression of the drug target protein results in an increase or decrease in expression of the drug target protein when a candidate drug is administered to the host cells as compared to the expression in host cells to which a candidate drug is administered but in which the drug target protein has not been introduced.] ← support.

2. (amended) The method of claim 1_2 wherein the [result of the protein expression is analyzed to identify a molecular target candidate compound] drug target protein expression is modulated when a candidate drug compound is administered to a host cell, in which the drug target protein has been introduced, thereby identifying a target of the drug candidate compound.] support.

7. (amended) A method for detecting a potential drug target protein, comprising:

modulating, by somatic gene transfer, expression of the drug target protein in host [selected] cells; [analyzing the result of expression of the target protein]

administering a candidate drug compound to the host cells; and,

determining the expression of the drug target protein expressed in the host cells.

14. (amended) The method of claim 7, wherein the drug target protein [is capable of specifically forming a binding] forms a complex with at least one other protein.

29. (amended) A method of mimicking one or more effects of a drug candidate compound in an identified somatic cell, tissue or organ of interest, the method comprising:

~~a)~~ modulating, by somatic gene transfer, expression of a [selected] desired drug target protein in [selected] cells; and,

administering to the cells a candidate drug compound; wherein,

the candidate drug compound modulates the expression of the drug target protein; and,

~~b)~~ analyzing the [result of] expression of the drug target protein as a result of administering the candidate drug compound; and,

[to] thereby [predict], predicting the effect of the drug candidate compound. have

31. (amended) The method of claim 30, further comprising [wherein the method further comprises use of a standard drug discovery strategy and use of the protein identified by the method]

culturing in medium a population of somatic cells, a tissue or an organ capable of expressing a recombinant nucleic acid segment encoding a drug target protein; and,

modifying the nucleic acid segment sufficient to modulate the result of expression of the drug target protein in the cells, tissue or organ; and,

introducing the modified nucleic acid segment into the cells, tissue or organ under somatic cell gene transfer conditions sufficient to express a modified drug target protein; and,

administering to the cells, tissue or organ, a candidate drug compound; wherein,

the candidate drug compound modulates expression of the modified drug target protein; and,

analyzing the expression of the modified drug target protein in cells, tissue or organ to which the candidate drug has been administered to determine potential drug target proteins.